Electronic Submission of Reg. Information, and Creating an Electronic Platform for Enhanced Information Management

Docket No. 2006N-0464

Public Hearing 12/18/06

Comments from Isis Pharmaceuticals, Inc

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ISIS

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1. Transition from Paper to Electronic

- FDA: Since January 1999, we have accepted the voluntary electronic submission of certain premarket applications. If you are not voluntarily submitting such applications electronically, what is the reason(s)?
- **Regulatory Operations perspective:**

  Sponsor has preferred from an operational standpoint to submit by paper only. There has not been a strong internal movement to change format, templates and retrain our staff in order to meet the requirements of an electronic submission. This can be attributed to limited resources and until recently, lack of expertise. It also was a matter of priorities.

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- FDA: Are you electronically submitting any portion of your premarket application? Is the portion specific to product type or premarket application?
- **Regulatory Operations perspective:**
  - **When Sponsor submits future new drug applications, our plan at this time is to submit electronically in the CTD format.**
  - **We plan to submit the entire CTD.**
- FDA: What are the major impediments to an all-electronic submission environment?
- **Regulatory Operations perspective:**
  - **Paradigm Shift**
  - **Cost of software**
  - **Development of Work Processes**
  - **Publisher training**
  - **Author training**

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- FDA: How can FDA best address these impediments?
- **Regulatory Operations perspective:**
  - **Clear requirements**
  - **Continued OIM communication**
  - **Shared best practices**
- FDA: Are there certain types of premarket applications or portions of applications that would be more difficult to submit electronically? Why?
- **Regulatory Operations perspective:**
  - **Based on current in-house expertise with past experience in an electronic submission environment, it was not more difficult to submit one portion than the other electronically.**

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- FDA: Are there specific issues related to electronic submission of premarket applications that are unique to small companies, academic institutions, and government agencies? If so, what are they and why are they unique?
- **Regulatory Operations perspective:**
  - **If FDA requires using XML for all electronic submissions, then for small companies the cost of software could be an issue**
  - **Integration of software for XML with EDMS systems such as Documentum, Livelink etc.**
  - **Viewing capabilities of the submission as it is being built for the organization outside of the regulatory department**

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- FDA: In addition to the sponsors of premarket applications, are there other sectors of FDA regulated industry that would have to make adjustments in business practices in an all-electronic submission environment? Please describe any such adjustments.
- **Regulatory Operations perspective:**
  - **CRO's**
  - **Pre-clinical laboratories**
  - **Trial sites**
  - **Partners contributing data/information**

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- FDA: In your opinion, what internal expertise is needed for firms to make the transition to an all-electronic premarket submission? Do firms have this expertise?
- **Regulatory Operations perspective:**
  - **Previous electronic submission experience, if available**
  - **Clear understanding of the requirements of the FDA for the electronic submission by the contributing project team**
  - **Best practice guidances set up within the company to assist the project team**
  - **Project management by the Regulatory lead for the submission**
  - **A clear development, review and editing plan – electronically and live meetings**
- **Most small firms do not have the first three points**

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- FDA: Is the labor market ready to accommodate industry's demand for such expertise to convert applications in an all-electronic submission environment?
- **Regulatory Operations perspective:**
  - **Not yet. Many companies will look to a third party company to format, publish, compile, QC and complete and submit their electronic submissions**
  - **In some cases, these third-party companies will continue to assist through the life-cycle of the drug**

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- FDA: Are there enough entities available to provide such services or tools in support of this effort? If not, how long would it take for these services to become available?
- **Regulatory Operations perspective:**
  - **Yes. However, industry views most software and tools as still "in development" as long as the FDA has not ultimately decided what the electronic life-cycle management picture is conclusively.**
  - **The service companies assisting in the electronic submission process continue to show promise and provide a level of comfort for some companies.**

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- FDA: How would an all-electronic submission environment benefit you?
- **Regulatory Operations perspective:**
  - **Once the initial business practices are changed to the electronic process, an all-electronic environment would benefit us in the following ways:**
    - **Lower error margin – due to the links in an electronic submission to the actual data, the chances are less likely that erroneous data would be included in the NDA**
    - **Increased quality – due to the tools for auditing the electronic submission and the ease of reviewing an electronic submission, your quality increases. Less chance for human error due to paper copies etc.**
    - **Savings of time and money – an in-house NDA saves the sponsor both time and money in resources, ease of reviewing, final preparation and final submission. It also contributes to continued savings due to ongoing amendments to FDA being electronic, no need for paper copies in house**
    - **Life-cycle management and record retrieval**

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2. Costs

- FDA: What do you estimate as the cost burden to you if all premarket applications and related documents are submitted electronically? What is the breakdown of the cost (e.g., software, programming, hardware, training)?
- **Regulatory Operations perspective:**
  - **Not able to estimate the cost section at this time**

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3. Time

- FDA: Based on your current method of preparation to submit applications, how much time would be required for preparation to submit the entire application in an electronic format; or a portion by an entity providing services related to the application?
- **Regulatory Operations perspective:**
  - **Not able to provide estimate at this time**

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- FDA: How long would it take you to prepare and submit an application electronically under the current format accepted by FDA for voluntary submissions?
- **Regulatory Operations perspective:**
  - **The answer to this is dependent on amount of pivotal trials, amount of patients, pre-clinical studies, i.e., the amount of data provided. It is limited by the authoring, review and editing portion of the process.**
  - **500 hours for a 505(b)2 after completion of the NDA authoring. A six person regulatory team, in coordination with Clinical, CMC, Data Management, Statistical and IT personnel worked on the NDA for 11 months.**

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- FDA: How much time would you need to make a smooth transition to a new electronic system?
- **Regulatory Operations perspective:**
  - **Four to six months depending on prioritization and resourcing**
- FDA: How would your estimated time differ for various product types or applications?
- **Regulatory Operations perspective:**
  - **Not able to estimate at this time**

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4. Implementation

- FDA: Should we consider an incremental phase-in implementation strategy for an all-electronic submission environment? Is so, what should the strategy include? What is the order of priorities for phasing in implementation?
- **Regulatory Operations perspective:**
  - **Incremental starting with premarket applications.**
  - **Highly specific guidances**
  - **OIM feedback opportunities**

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- FDA: Are the tools and formats currently available for FDA electronic submissions adequate? If not, why? What is needed?
- **Regulatory Operations perspective:**
  - **Tools and formats currently are adequate**
  - **Need to work on continuous improvement**
  - **Simplified established formats are optimal and reduce training expenses**

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- FDA: Would issuing guidance be useful in helping with the transition? If so, what topics would you like addressed?
- **Regulatory Operations perspective:**
  - **Guidance documents for the transition would be very helpful**
  - **Utilization of experienced industry stakeholders collaborating on writing guidance documents**
  - **Separation of programming language from operational language in the guidance documents is preferred.**
  - **Straightforward and simple communication in the guidance documents will enable more sponsors to gain in-house expertise**